REMARKS

Claims 1-9 and 19-20 are canceled and claims 13-17 are amended herein. Claims 10-12, 18 and 21-25 were previously canceled. Upon entry of the Amendment claims 13-17 will be all of the claims pending. No issues of new matter are presented.

I. Response to Claim Objections

Claims 19 and 20 were objected to as dependent upon a rejected claim. Claims 19 and 20 are canceled herein and therefore the rejection is moot. Accordingly, Applicants respectfully request withdrawal of the objection.

II. Response to Claim Rejections Under 35 U.S.C. § 112, 1st Paragraph

Claims 13-17, 19 and 20 were rejected as allegedly being non-enabled. The Examiner asserts that the claims are only enabled for direct injection of the composition. Applicants have amended claims 13-17 to recite that the method of administration is by direct injection. Claims 19 and 20 are canceled herein and the rejection as to claims 19 and 20 is moot. Accordingly, Applicants respectfully request withdrawal of the rejection.

III. Response to Claim Rejections Under 35 U.S.C. § 112, 2nd Paragraph

Claims 13-17 are rejected under 35 U.S.C. § 112, 2nd paragraph, as allegedly being incomplete for failing to recite the outcome of the method. Applicants have amended claims 13-17 to recite the respective outcome of the method. Accordingly, Applicants respectfully request withdrawal of the rejection.

IV. Response to Claim Rejections Under 35 U.S.C. § 102(e) over Mann et al

Composition claims 1-9 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Mann et al (U.S. Patent No. 6,199,544).

Claims 1-9 are canceled herein, thereby rendering the rejection moot. Accordingly, Applicants respectfully request withdrawal of the rejection.

V. Response to Claim Rejections Under 35 U.S.C. § 102(b) over WO 97/07824 (WO '824)

Claims 1-9 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by WO '824.

Claims 1-9 are canceled herein thereby rendering the rejection moot. Accordingly, Applicants respectfully request withdrawal of the rejection.

VI. Response to Claim Rejections Under 35 U.S.C. § 102(e) over Morishita et al

Claims 1-9 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Morishita et al.

Claims 1-9 are canceled herein thereby rendering the rejection moot. Accordingly, Applicants respectfully request withdrawal of the rejection.

VII. Response to Claim Rejections Under 35 U.S.C. § 102(e) over copending App. No. 09/660,522

Claims 1-9 were provisionally rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by copending Application No. 09/660,552, which is a continuation of U.S. Patent No. 6,248,722.

Claims 1-9 are canceled herein thereby rendering the rejection moot. Accordingly, Applicants respectfully request withdrawal of the provisional rejection.

VIII. Response to Claim Rejections under 35 U.S.C. § 102(f) over U.S. Patent No. 6,248,722

Claims 1-9 were rejected under 35 U.S.C. § 102(f). The Examiner states that U. S. Patent No. 6,248,722 discloses the same invention as presently claimed in claims 1-9, but has a different inventive entity. The Examiner requests clarification.

Claims 1-9 are canceled herein thereby rendering the rejection moot. Accordingly, Applicants respectfully request withdrawal of the rejection.

IX. Response to Claim Rejections under 35 U.S.C. § 102(f) over U.S. Patent App. No. 09/660,522

Claims 1-9 were provisionally rejected under 35 U.S.C. § 102(f) over U.S. Patent Application No. 09/660,522.

Claims 1-9 are canceled herein thereby rendering the rejection moot. Accordingly, Applicants respectfully request withdrawal of the provisional rejection.

X. Response to Claim Rejections Under 35 U.S.C. § 103

Claims 1-9 and 13-17 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Isner et al (U.S. Patent No. 6,121,246 or WO 97/14307) and Morishita et al (U.S. Patent No. 6,248,722), in view of Ghodsi et al (Hum. Gene Ther. 1998;92331-40).

According to the Examiner, Isner et al teach a composition including all of the components of claims 1-9, except for specifying that the liposome is an HJV liposome. However, according to the Examiner, Morishita et al teach an HJV-liposome carrying an HGF gene. The Examiner' s position is that one of ordinary skill in the art having Morishita et al would readily substitute the HJV-liposome of Morishita et al for the liposome of Isner et al in order to achieve the presently claimed composition.

As to method claims 13-17, the Examiner asserts that Isner et al teach treating ischemia by local injection to more than one site in the ischemic tissue, which in the case of cerbrovascular ischemia is the brain tissue. The Examiner's position is that Isner et al and Morishita et al together teach treating ischemia by local injection of the claimed composition. The Examiner further asserts that HGF has many pharmaceutical activities and therefore could be used to treat many different diseases such as nervous disorders and arterial diseases, which encompass cerbrovascular disorders. The Examiner recognizes that neither Morishita et al nor Isner et al teach injection into the subarachnoid space. However, according to the Examiner, Ghodsi et al teach introducing an adenoviral vector into the central nervous system via direct injection into the subarachnoid space. Accordingly, the Examiner asserts that one of ordinary skill in the art would readily use the compositions of Isner et al and Morishita et al to treat cerbrovascular ischemia and other cerebrovascular disorders, and in view of Ghodsi et al, one would administer directly into the subarachnoid space, in order to achieve the claimed methods.

Applicants respectfully traverse the rejection and submit that the cited references do not teach or suggest the presently claimed methods.

The Present Inventions

The inventions of amended claims 13 to 17 relate to methods for treating or preventing cerebrovascular disorders or reduced blood flow, for promoting cerebral angiogenesis, and for suppressing neuronal death in the brain or apoptosis of nerve cells, comprising an HGF gene and/or a VEGF gene in the form of HJV-liposomes by direct injection into the subarachnoid space in humans.

Differences Between the Present Inventions and the Cited References

Although Isner et al and Morishita et al teach treating ischemia by local injection of a HGF or a VEGF gene, neither Isner et al nor Morishita et al teach injection into the subarachnoid space. Further, although Ghodsi et al teach introducing an adenoviral vector into the subarachnoid space, Ghodsi et al use β-glucoronidase gene, and do not teach use of the HGF gene or VEGF gene in the form of HJV-liposomes.

The HGF gene or VEGF gene in the form of HJV-liposomes used in the present invention is a non-adenoviral vector, which is clearly different from the adenoviral vector used in Ghodsi et al.

Furthermore, Ghodsi et al teach treating mucopolysaccharidosis, but teach nothing of treating or preventing cerbrovascular disorder or reduced blood flow, promoting cerebral angiogenesis, or suppressing neuronal death in the brain or apoptosis of nerve cells. As stated in Ghodsi et al, mucopolysaccharidosis is a classic lysosomal storage disease. Mucopolysaccharidosis is characterized by the excretion of mucopolysaccharides into urine or the infiltration of mucopolysaccharides into connective tissues, resulting in various disorders in bones, cartilage and connective tissues. Thus, mucopolysaccharidosis is fundamentally different from the diseases treated with HGF or VEGF protein or gene.

In view thereof, one of ordinary skill in the art would not have been motivated to combine Isner et al and Morishita et al with Ghodsi et al with a reasonable expectation of success in achieving the presently claimed invention.

Accordingly, Applicants respectfully request withdrawal of the rejection.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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